

## REMARKS

Applicants appreciate the Examiner's thorough and detailed examination of the present application as evidenced by the Office Action dated March 27, 2008 (hereinafter, "Office Action"). Applicants hereby request further consideration of the application presenting pending Claims 1-28, 34 and new Claim 37 in view of the claim amendments above and the comments that follow.

### Claim Rejections Under 35 U.S.C. §112

As stated in the Office Action, Claims 1-24 and 34 stand rejected under 35 U.S.C. §112, second paragraph, as being indefinite. *See* Office Action, page 2. Claims 2-24 and 34 stand rejected similarly for depending from a rejected base claim. *See* Office Action, page 3. Claims 1, 11 and 26 have been amended as presented herein in order to address the Examiner's concerns. Accordingly, Applicants respectfully submit that the rejection of pending Claims 1-24 and 34 have been overcome, and Applicants respectfully request that this rejection be withdrawn.

### Claim Rejections Under 35 U.S.C. §102

Applicants respectfully submit that a finding of anticipation requires that there must be *no difference* between the claimed invention and the disclosure of the cited reference as viewed by one of ordinary skill in the art. *See Scripps Clinic & Research Foundation v. Genentech Inc.*, 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001, 1010 (Fed. Cir. 1991) (Emphasis added). Additionally, the cited prior art reference must be *enabling*, thereby placing the allegedly disclosed matter in the possession of the public. *In re Brown*, 329 F.2d 1006, 1011, 141 U.S.P.Q. 245, 249 (C.C.P.A. 1964) (Emphasis added). Thus, the cited reference must adequately describe the claimed invention so that a person of ordinary skill in the art could make and use the invention.

**A. Claims 1-22, 27 and 28**

Claims 1-22, 27 and 28 stand rejected under 35 U.S.C. §102(b) as being anticipated by Chaudhuri et al. (hereinafter "Chaudhuri"). *See* Office Action, page 4. As presented herein, Claim 1 has been amended to clarify that the methods of the present invention include ***monitoring changes in xenograft metabolism*** and further includes measuring at least one parameter of a selected biochemical/ physiological response associated with the reporter molecule or reporter gene that is ***secreted into the blood or excreted in a body product***. Additionally, new dependent Claim 37 recites a step ***wherein multiple measurements are made over a protracted period of time***. Support for the claim amendment and new claim can be found in the specification as originally filed, for example, page 8, line 27 through page 9, line 2 and page 5, lines 25-27, respectively.

In contrast, Chaudhuri merely employs an adenoviral vector to deliver a CMV-GFP reporter to estimate uptake of a therapeutic gene delivered by the adenoviral vector. There is no teaching, suggestion or enablement regarding use of measurement systems to assess or measure changes in tumor metabolism, and certainly not with respect to a method allowing multiple measurements that are made over a protracted period of time.

Accordingly, Applicants respectfully submit that Claims 1-22, 27 and 28 are not anticipated by Chaudhuri.

**B. Claims 1-5, 7-9, 13-23, 27 and 28**

Claims 1-5, 7-9, 13-23, 27 and 28 stand rejected under 35 U.S.C. §102(b) as being anticipated by Lin et al. (hereinafter "Lin"). *See* Office Action, page 4.

Lin merely observes the effects of cisplatin treatment on expression of xenograft tumors expressing a GADD153-GFP reporter. However, to assay reporter expression, the xenograft tumors had to be excised for flow cytometric analysis. *See* Lin, page 559. Applicants respectfully submit that Lin fails to teach, suggest or enable a method for noninvasive monitoring of reporter molecules secreted into the blood or excreted in a body product, such as urine, and further allowing multiple measurements to be made over a protracted period of time to monitor changes in xenograft metabolism.

Accordingly, Applicants respectfully submit that Claims 1-5, 7-9, 13-23, 27 and 28 are not anticipated by Lin.

**C. Claims 1-5, 7-9, 13-22, 24, 25, 27, 28, and 34**

Claims 1-5, 7-9, 13-22, 24, 25, 27, 28, and 34 stand rejected under 35 U.S.C. §102(e) as being anticipated by U.S. Patent No. 6,926,890B2 to Vogelstein et al. (hereinafter "Vogelstein"). *See* Office Action, page 5.

Vogelstein merely uses a CMV-hCGB reporter to monitor tumor growth, i.e., cell numbers. See, for example, Lin at column 3, lines 57-60, which state, "[t]he inventors have found that the level of the exogenous protein in the urine is proportional to the number of viable recombinant tumor cells in the animals." Lin does not teach, suggest or enable use of the reporter molecule in determining changes in tumor ***metabolism***.

Accordingly, Applicants respectfully submit that Claims 1-5, 7-9, 13-22, 24, 25, 27, 28, and 34 are not anticipated by Vogelstein.

**D. Claims 1-5, 7-9, 13-22, 24-28, and 34**

Claims 1-5, 7-9, 13-22, 24-28, and 34 stand rejected under 35 U.S.C. §102(e) as being anticipated by WO 98/056936 to Risau et al. (hereinafter "Risau"). *See* Office Action, page 6. Risau merely relates to the use of xenograft tumors expressing a VEGF-LacZ reporter to monitor the effects of EF5 treatment. Again, tumors were excised to allow X-Gal staining (See pages 34 and 35). However, Risau does not teach, suggest or enable a method for monitoring changes in xenograft metabolism including noninvasive monitoring of reporter molecules secreted into the blood or excreted in a body product, such as urine, and further allowing multiple measurements to be made over a protracted period of time to monitor changes in xenograft metabolism.

Accordingly, Applicants respectfully submit that Claims 1-5, 7-9, 13-22, 24-28, and 34 are not anticipated by Risau.

At least in view of the foregoing, Applicants respectfully submit that the pending claims are not anticipated by the cited references, and Applicants respectfully request that these rejections be withdrawn.

### CONCLUSION

In view of the foregoing amendments and remarks, Applicants respectfully request that all outstanding rejections to the claims be withdrawn and that a Notice of Allowance be issued in due course. The Examiner is invited and encouraged to contact the undersigned directly, if such contact will expedite the prosecution of the pending claims to issue. In any event, any questions that the Examiner may have should be directed to the undersigned, who may be reached at (919) 854-1400.

Respectfully submitted,



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### CERTIFICATION OF TRANSMISSION

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Betty-Lou Rosser